

Recollections of My Young Days —The Pleasure of Creation—

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I was bashful by nature. In elementary school, I was enthusiastic about painting pictures, posters, and calligraphy, and making butterfly specimens and models. When I entered the middle school of Seikei Gakuen, I was fortunate to have good teachers and friends. Prof. Kusatao Nakamura taught us the “Preciousness of the pureness of heart”, which is the principle of my life. After World War II, school classes reopened. I was deeply moved by the lecture of botany by Prof. Fumio Maekawa, and had a notion that I should like to make research my lifework. I went to high school and had the worries of my life. During that time, it was the book *Gakusei ni atau* by Prof. Eijirou Kawai, and a speech by Prof. Tadao Yanaihara, that sustained my heart. In 1953, I entered the postgraduate course of the University of Tokyo, and received the guidance of Prof. Yuichi Ochi. This matter was decisive for my life. First of all, I developed a new medium, BL agar, for culturing intestinal bacteria, and then I discovered that Bifidus bacteria was one of the predominant organisms in human adults. This discovery became the basis of my research until today. For two years from 1964, I studied abroad in Germany and made good friends, to whom I owe an inestimable debt of gratitude. After returning to Japan, I discovered a number of rules governing the intestinal ecosystem. Thus, a new interdisciplinary field, intestinal bacteriology, was established. Subsequently, I discovered the health effects of fermented milks and oligosaccharides and proposed “biogenics”. I firmly believe that the fruit of creation is granted as a result of endeavoring with a pure heart.

Key words: recollection, creation, teachers, friends, intestinal microbiota

UNTIL DETERMINING TO BECOME A RESEARCHER

Birth

I was born in Ichikawa in 1930. I had an educationally-minded mother, and my father worked for a pharmaceutical company in Tokyo. He was a man of few words, didn't scold or get angry, took a stroll in the neighborhood on Sundays and devoted himself to composing *haiku* poems. I was introverted by nature, and I inherited this character from my father.

School in the sand pit

My elder brother entered elementary school when I was three years old. I dragged an old curtain and a bamboo pole from a storeroom and made a tent in the sand pit in the backyard. I asked my mother to make lunch, as I was going to the “school in the sand pit” and played alone. This was the start of “the pleasure of creation”.

I was bullied as soon as I entered kindergarten when I

became 5 years old. I was taught the strictness of living. I developed nephritis due to stress, and left kindergarten. I recovered next year and was able to enter elementary school.

Absorbed in creation in the elementary school

In the elementary school, shy by nature, inner direction began to lead me more and more, and I became absorbed in painting my favorite pictures, posters, and calligraphy, making models, insect-collecting, and scientific experiments, and often won prizes (Fig. 1). Exhibiting the work, and accepting the prizes were a great pleasure for me, and became the support of my heart. I avoided associating with friends, and became absorbed by collecting insects alone. It became my custom to wander which was something of my father's character.

In the spring vacation of the fifth grade of elementary school, I spread a mat in a sunny part of the backyard. I experimented with charcoal gas generation using a spirit lamp, test tube, cork stopping, glass tube, and half-split chopsticks. I succeeded. The excitement is still unforgettable, even now.

My educationally-minded mother often scolded me with “Why do you not study?” However, she said “Do as

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Fig. 1. Prize (paper weight) of an exhibition in Army Anniversary Memorial Day.



Fig. 2. Campus of the Seikei Gakuen.

you please” and swept my room, when I became absorbed in model-making.

My father was likely to have had a presentiment that I would be such a child. He made the wish, “There will be no complaints about him”, and gave me the name “Tomotari” taken from Lao-tse’s teaching, “Whoever knows sufficient is rich”. However, I have difficulty to enter the high school, if I devote too much to knowing sufficient, and out of parent love, my parents let me enter Seikei Gakuen (Fig. 2) which had a seven year high school system.

Meeting with good teachers and friends at Seikei Gakuen

“A peach and the plum say nothing, but a lot of people gather yearning the flower and fruit” is the origin of the name “Seikei”. At Seikei high school a small number of students received a liberal education according to their ability, which valued their personality. It was immeasurable experience of my life that I was able to meet good teachers and friends and be influenced by them.

Prof. Shin Kusakawa (Fig. 3), who is well-known for the children’s song “*Yuu-yake, ko-yake*”, gave me the opportunity to listen to and play classical music.

At that time, militarism was in full swing. Because I was a weak-looking student who was unacceptable to the military, the instructor of military drill scolded me, “Your salute is not good. Your thought is the principle of freedom, equality, and philanthropy”. When I saluted him, I thought, “I flatly refuse to accept militarism and military force”.

Fortunately, I was able to learn the “preciousness

of living by single-mindedness” from Prof. Kusatao Nakamura, a *haiku* poet, (Fig. 4). At the end of the Japanese literature class of the first grade, the teacher said to us, “Please live as purely as possible forever, because it can be done at anytime, even if you think that you want to become an adult”. These words had a decisive influence on forming my personality and became the creed of my life.

Yearning to be in the aeronautics department and father’s death

The fighters were arriving and departing from the military airport in Chofu near the Seikei high school every day. I was fascinated by the beautiful forms and excellent performance of the fighters, and I enjoyed making models of the new star fighters while dreaming that I would enter the aeronautics department of the university in the future. I read scientific articles on fighters and rocket. I also made a crystal radio for the blackout, and listened to a lot of classical music and was deeply impressed.

My father died of acute pneumonia before the end of the war. I was just 15 years old at that time, and experienced a big shock from this unexpected event. However, a paternal uncle said that he would help meet all the school expenses of my brothers. At this time, I was strongly touched by the love I received from a relative.

End of the War ; School classes reopen

I heard the acceptance of the Potsdam Declaration and the unconditional surrender broadcast of the Emperor with technological officers in the Navy Institute of Technology, my student mobilization place, at 12:00 on August 15, 1945. The joy that the fierce war had ended,



Fig. 3. Prof. Shin Kusakawa.

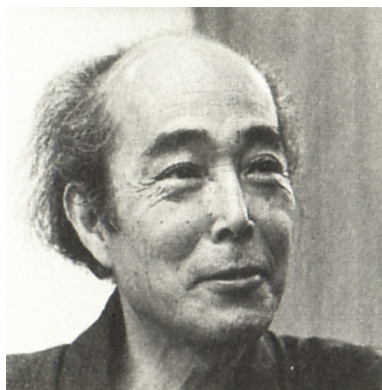


Fig. 4. Prof. Kusatao Nakamura

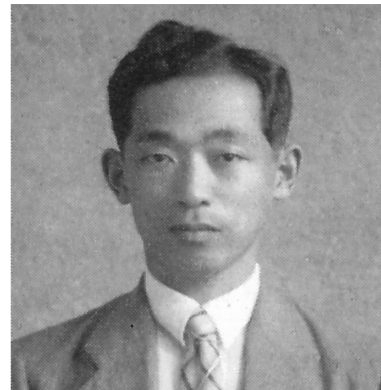


Fig. 5. Prof. Fumio Maekawa.

and the sense of relief from not having to go to war filled my heart. After an interruption of about two years, school classes were reopened. We, who desired to learn, listened attentively to the lectures reveling in the peace and the disappearance of military drill. I was deeply impressed by the botany lectures given by Prof. Fumio Maekawa (Fig. 5).

Entering the advanced course

When starting the advanced course of the Seikei high school, I wanted to go to the aeronautics department of the university in the future, and entered the course 1 of science. However, the aeronautics department was temporarily abolished by GHQ and there was no expectation of its revival. I changed to the course 2 of science at the second grade. There, it was possible to listen to the lectures of Prof. Maekawa again. Prof. Maekawa came as a docent to the Seikei high school, and taught with zeal the interest of research to us who were 20 years or more his younger, kindly and politely including a new finding on many plant taxonomies. All of the 10 hours of lectures made a deep impression on me, which I had not experienced till then. I decided that I wanted to do systematic botany as my lifework, if possible. Prof. Maekawa was indeed the person who gave me the chance to choose the way of a researcher. The thought of Prof. Maekawa continues to exist in my bacterial taxonomy. I fully realize now, how important for my life the education received in high school was.

Worries of youth and conversion to Christianity in Kuriyama in early spring

My high school student days were fraught with anxieties. I felt doubt in myself about the self-centered thoughts that it was natural to be received from other

people. I noticed that it was I who had not thought that we had to thank God or persons till then.

At that time, however, for the support of my heart, answering worry, there was the book, *Gakusei ni atau* (For a Student) written by an idealist Prof. Eijiro Kawai [1] and a book by Prof. Tadao Yanaihara (Fig. 6). From *Gakusei ni atau* I was taught “the personality is the main constituent which harmonized and united is the truth, goodness and beauty, and the search for the truth, goodness and beauty is the highest value of life”. From the book [2] by Prof. Yanaihara I was taught “live as the mission of life which is determined, and God will surely protect the person who does the right thing”. At that time, I decided to convert to Christianity.

When I wandered in a deserted wood where sunshine filtered through the foliage near the Kuriyama water purification plant in Ichikawa Konodai (Fig. 7) in the morning and looked back on my life, I demanded help from the sky. I was informed that I was too self-centered,



Fig. 6. Books by Prof. Eijiro Kawai and Prof. Tadao Yanaihara.

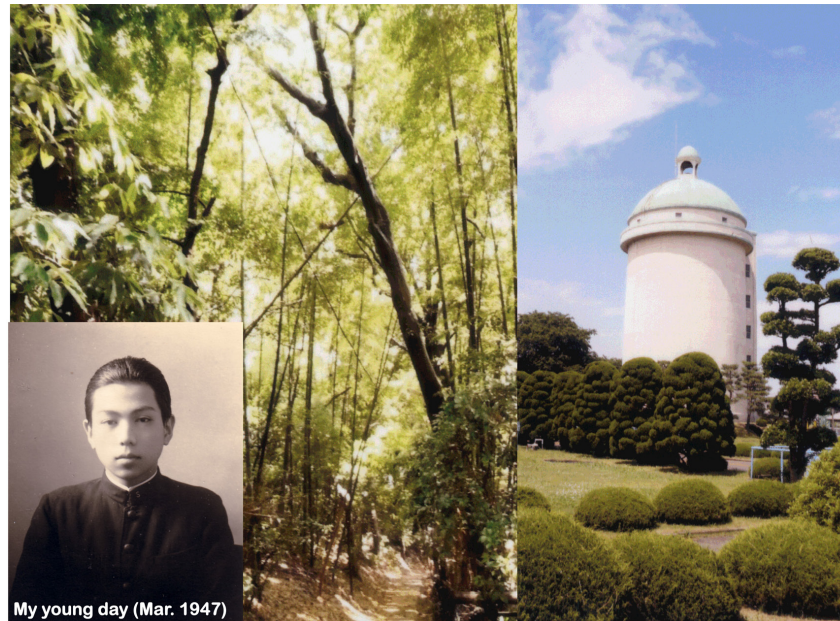


Fig. 7. Decided a way of my life in the wood of Kuriyama, Ichikawa Konodai

and my heart was strangely healed. I took note of the fact that everyone is different in figure, character, and ability, which were already given from God by nature, and I took very serious thought that I should live a straight life while accepting obediently fate, enduring the inequality and unfairness given from Heaven, and making the best use of my own personality and respecting the personality of another person. At that time a feeling of gratitude to God, nature and society sprang up and overflowed in my heart, and I reformed. It was early spring, and I was 18 years old.

Impressed by Beethoven's music I took violin lessons from Prof. Yozo Iwasaki

In those days, I was impressed and given hope and courage by the music of Beethoven who reached the world which was closer to God, even though his life was filled with loneliness and suffering. At that time I wanted to play Beethoven's music by myself, and I decided to take violin lessons from Prof. Yozo Iwasaki (Fig. 8) of the Tokyo University of Arts. I also served as violin player and Director of an amateur orchestra (Fig. 9).

It was creation to play and listen to classical music, and it helped me to develop the intuitions and ideas in the process of creation in research. Having served as the orchestra director was useful for guidance and management of the laboratory in later years.

Entering the University of Tokyo and deciding to live as a researcher

I entered The University of Tokyo in 1950 and was able to meet good teachers and good friends again. It was an actual feeling that the lectures were so interesting when a science is specialized at the university. In the third grade, I entered the Animal Physiology Laboratory to begin my graduation thesis. At this time, I was able to experience how interesting research life was, and understood being a researcher was the best occupation in which to be able to do anything I like. So I decided to enter the graduate school and live as a researcher.

POST-GRADUATE RESEARCHER

1953–1958: Establishment of the foundation of the intestinal microbiota research

I entered the Bacteriology Laboratory and I was directed to study the intestinal flora of the chicken by Prof. Yuichi Ochi (Fig. 10).

Before starting the research, I examined nearly 200 papers in the literature on intestinal microbiota and summarized them. I reported my findings to the researchers of the laboratory. This work became the keynote of my master thesis, and was later published in the Journal of Japanese Veterinarian Association as a review, in three volumes.

My research started with the development of a culture



Violin Schools & Etudes
 Ono Anna, Violin Scale
 Sevcik, Exercises in Double Stopping
 Hohman, Practical Violin School
 Dont, 24 Etudes & Caprices Op. 35
 Kayser, 36 Etudes Op. 20
 Kreuzer, 42 Etudes
 Rode, 24 Caprices

Repertoires

Vivaldi, Concerto in a
 Home Sweet Home Theme and Variation
 Brahms, Hungarian Dances No. 6
 Corelli, La Folia
 Pugnani, Preludium & Allegro
 Falla, Danse espagnole
 Händel, Sonata No. 4
 Beethoven, Sonata No. 5 in F
 Viotti, Concerto No. 23 in G
 Nardini, Concerto in e
 Bach, Concerto No. 1 in a
 Bach, Chaconne in d
 Mozart, Concerto No. 3 in G
 Mozart, Concerto No. 4 in D
 Mozart, Concerto No. 5 in A
 Beethoven Romances in F
 Beethoven Concerto in D, Cadenzas by Kreisler
 Mendelssohn, Concerto in e op. 64
 Bruch, Concerto No. 1 in g op. 26
 Vieuxtemps, Fantasie Appassionata in G op. 35
 Vieuxtemps, Concerto No.4 in d op. 31
 Veracini, Sonata in e
 Lalo, Symphonie espagnol op. 21
 Wieniawski, Legende op. 17

Fig. 8. Receive violin lessons from Prof. Yozo Iwasaki.

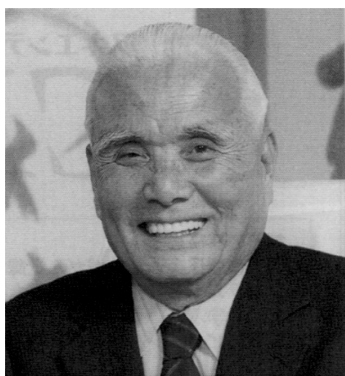


Fig. 10. Prof. Yuichi Ochi.

Repertoires (1951 ~ 1958)

Haydn, Symphony No. 94 in G
 Haydn, Symphony No. 100 in g
 Haydn, Symphony No. 101 in D
 Mozart, Symphony No. 39 in E b
 Mozart, Symphony No. 40 in g
 Mozart, Symphony No. 41 in C
 Beethoven, Symphony No. 1 in C
 Beethoven, Symphony No. 5 in c
 Beethoven, Symphony No. 6 in F
 Schubert, Symphony No. 8 in b
 Beethoven, Overture Egmont
 Mozart, Overture Die Zauberflöte
 Mozart, Overture Le Nozze di Figaro
 Mendelssohn, Violin Concerto in e
 Mozart, Piano Concerto No. 20 in d
 Mozart, Piano Concerto No. 26 in D
 Haydn, Piano Concerto in D
 Beethoven, Piano Concerto in E b
 Grieg, Piano Concerto in a
 Liszt, Piano Concerto No. 1 in E b



Fig. 9. A scene of general program by Ichikawa Symphony Orchestra.

method for the intestinal flora. I developed BL agar (Fig. 11) and discovered that Bifidus bacteria had habitation as the predominant bacteria in the intestine of human adults. At that time, I was convinced that Bifidus bacteria must be important for health. This developed into my research into the intestinal microbiota of humans, which I started ten years later, and it became the basis of my research until today.

When I presented my findings to the Annual Meeting of Bacteriology, I was contradicted, “Mitsuoka classifies another bacteria as Bifidus bacteria”. The reason for this was that my discovery was not common sense in medical bacteriology at that time. Most of the textbooks of medical bacteriology described Bifidus bacteria as the predominant flora in the infant intestine, while

Lactobacillus acidophilus was the most common bacteria in the adult intestine.

In the first step of my research, I cultured the intestinal contents of chickens using BL agar, and discovered that lactobacilli were the predominant bacteria. However, it took a long time to identify *Lactobacillus*, because the strain distributed as the standard (reference) strain of *L. acidophilus* from culture collections in Japan was not *L. acidophilus* but *L. casei* at that time. This experience taught me that the standard strain is not always correct. I classified lactobacilli isolated from the gastrointestinal tracts of various animals, including chickens, yoghurt, and agricultural products and proposed that the bacterial group classified as *Lactobacillus bifidus* should be classified as the genus *Bifidobacterium* (Orla-Jensen, 1924) [3].

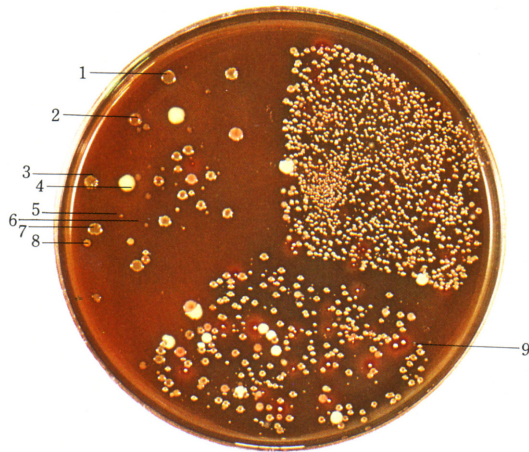


Fig. 11. Discovery of BL agar and predominant flora of bifidobacteria in an adult fecal specimen.
1,2,3,7: *Bifidobacterium*, 4: *Megasphaera elsdenii*, 5,6: *Bacteroides*, 8: *Eubacterium*, 9: *Veillonella*

1958–1964: Member of the Institute of Physical and Chemical Research

In 1958 I entered the Institute of Physical and Chemical Research (Riken), where Prof. Ochi concurrently served as the Principal Scientist. Prof. Ochi told me to examine the culture method of rumen flora. There, I introduced the anaerobic roll-tube method developed by R. E. Hungate [4] for the isolation of cellulolytic anaerobic bacteria in the rumen. This culture method was applied to study of the intestinal flora and made possible the growth of fastidious anaerobes of humans and animals. This further led to the development of the plate-in-bottle method.

Because there was no facility which kept chickens at the Institute, I made a chicken house at my house, and conducted the cultural analysis of the main components of the intestinal flora of chickens, from chicks till hens. I discovered that just hatched chicks were germ-free at all levels of the intestinal tract. As the chicks grew older, the flora changed gradually, and I found that the flora of the intestine except for the cecum becomes established in chicks 9–13 days after feeding, and that the flora of the cecum were established later, after 23–32 days of feeding. In 1964, we published this fact in *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene*, I Orig. [5]. This knowledge was not in accordance with the common knowledge of that time, and created a big sensation outside Japan, leading to an interchange with Dr. Ella M. Barnes in England.

1964–1966: Studying abroad in Berlin

I went to study at the Department of Food Hygiene,



Fig. 12. Free University of Berlin (West), Veterinary Faculty, Institute of Food and Meat Hygiene.

Veterinary Faculty, Free University of Berlin (Fig. 12) as a scholarship student of the Alexander von Humboldt Foundation from September 1964 to August 1966, and was able to perform a taxonomic study of lactobacilli and bifidobacteria under Professor M. Lerche, Prof. H. J. Sinell, and Dr. G. Reuter.

I learnt the model of “Germanism” and the line of steady thinking and the technique of bacterial taxonomy. I made a life in the laboratory together with my German colleagues and was deeply impressed. Germanism was still alive in spite of the defeat in war: the strong zeal to the search for the invisible or indefinite things, logical planning, searching accurately and thoroughly. Further, I personally experienced the health effect of yogurt (Fig. 13), and thought that it was necessary to study the health effect of fermented milk.

In addition, I was able become acquainted with first-rank scholars, such as Dr. E. Barnes of the British National Food Institute, Dr. H. Haenel of the National Institute of Nutrition, East Germany, Dr. M. Coates of the National Dairy Farming Research Institute, U.K., and Dr. Savage of the University of Illinois, U.S.A. These scholars cooperated and actively supported my next study. I accepted invitations to become a member of the International Taxonomic Subcommittee on *Lactobacillus* and *Bifidobacterium* (Fig. 14) and a member of the International Taxonomic Subcommittee on the Gram-negative Anaerobic Rods (Fig. 15), and was able to participate in the collaborative investigations of these committees.

1966–1970: Return home and commencement of government-industry cooperative investigations

I returned home and the multipoint inoculator for identification of 12 bacterial strains was developed immediately. This device became powerful tool for the



Fig. 13. Experience of healthy effect of yoghurt at lunch time of the Institute.



Fig. 15. Members of Taxonomic Subcommittee on Gram-negative Anaerobic Rods.



Fig. 14. Members of Taxonomic Subcommittee of Lactobacillus and Related Organisms.

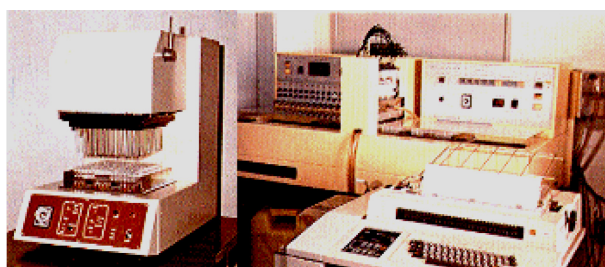


Fig. 16. Development of multipoint inoculator and automatic multipoint pH meter.

identification of bacteria. Afterwards, it was used in the successful development of an automatic identification device for 270 strains of bacteria (Fig. 16).

A lot of research workers from company institutes, universities, and hospitals came together, when I developed the culture method for comprehensive analysis of intestinal flora (Fig. 17) and the automatic identification device. This was the genesis of industry-government-university joint research. People called it the “Mitsuoka school” (Fig. 18). The researchers learned newly developed research methods, as a theme of the subject brought respectively. At that time I made a rule. The rule was to treat both the staff members of the Institute of Physical and Chemical Research and the research workers from industries or hospitals without discrimination and to allow them to behave freely in helping each other in the laboratory, but unjust acts, cunning acts, and oppressive attitudes were prohibited.

It was a happy and pleasant time sharing the pleasure of life with each other. Research workers took the results of research back to their institutes, and used them in later research and development.

At that time, the composition of the intestinal flora of various animals and the taxonomy and ecology of intestinal lactobacilli and bifidobacteria of various animals were being studied. Furthermore, the study of the proliferation and colonization of the bacteria administered into the intestine was carried out using germ-free animals. I thought how to further advance research on intestinal flora, and proposed a hypothesis “Relationships between intestinal flora and health” (Fig. 19) [6]. This was my work hypothesis, and I aimed the development of my subsequent research on the basis of this idea.

1971–1980: Discovery of the ecological rules governing intestinal flora and the establishment of intestinal bacteriology

Ecological rules related to individual variation, age-related difference in human intestinal flora (Fig.

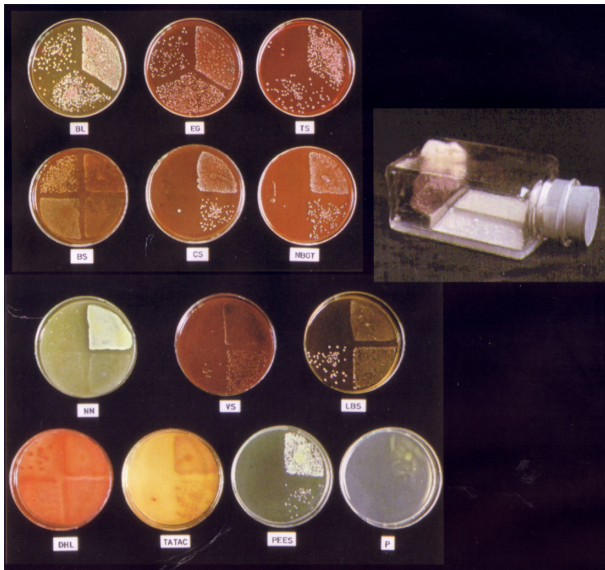


Fig. 17. Cultural method for comprehensive analysis of intestinal flora.



Fig. 18. Members of Mitsuoka School.

20), and the colonization and transmission of infantile bifidobacteria were discovered during this period [7-11]. Furthermore, the effect of feeding pasteurized sour milk on longevity, transplantable tumors, and intestinal flora in mice was studied, and it became clear that the

average life-span of mice fed pasteurized sour milk was 8% longer than that of a control group, and the counts of bifidobacteria in the intestinal flora of the mice fed with sour milk were 10 times higher than those fed with either whole milk or the control diet [12].

At this time, I judged that a new scientific field, intestinal bacteriology, was able to be established, and published *Chonai saikin no hanashi* (Intestinal Bacteria and Health) [7] and *Chonaikin no sekai* (A Color Atlas of Anaerobic Bacteria) [8].

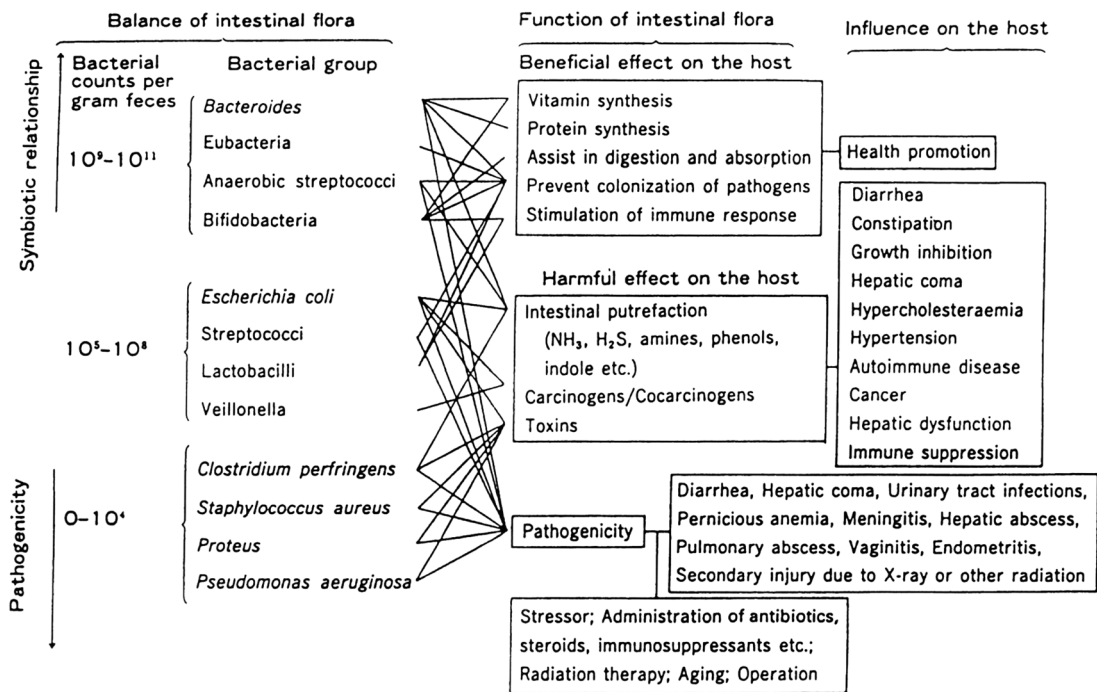


Fig. 19. Relationship between intestinal flora and health (Mitsuoka 1969).

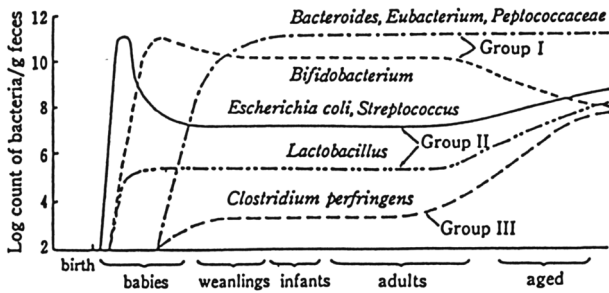


Fig. 20. Changes in fecal flora with aging (Mitsuoka 1978).

1981–2012: The effect of functional foods and the functional mechanism

On the basis of my research results for intestinal flora, I proposed a new concept, biogenics, and the functional mechanism of functional foods (Fig. 21). Furthermore, I pointed out that the maintenance of bio-homeostasis between the immune system, nervous system, and endocrine system was important as an action mechanism of functional foods (Fig. 22) [9–11]. Subsequently, I published the book *Kenko choju no tameno shokuseikatsu* (Eating habits for healthy longevity) [12].

Sixty years had passed since I had determined to become a researcher. In the meantime I had been awarded a lot of prizes for the fruits of creation (Fig. 23). I wish to express my gratitude for these awards.

CREATION AND THE WAY OF LIFE OF A RESEARCHER

Process of creation

Learning is an act that devotes itself to the search for truth, and art is an act that devotes itself to the search for beauty. Both have much in common with each other regarding the act called “creation”. In the act of the search for truth and beauty, a pure heart and the energy to gush out are required.

At each stage in the process of the creation, intuition becomes an important factor. Intuition is a mysterious phenomenon which appears suddenly in the process for the search of the truth with a pure heart by a person who has an innate talent. Looking at a scenery of nature or listening and performing good music are effective way of inspiring intuition.

In research, each stage from the selection of the research theme, the accomplishment of the research, and the summary of the result, to the evaluation of the research have importance (Fig. 24).

At the stage of selection of the research subject, the collection of relevant literature is carried out, and doubts about the prevailing common sense and preconceptions

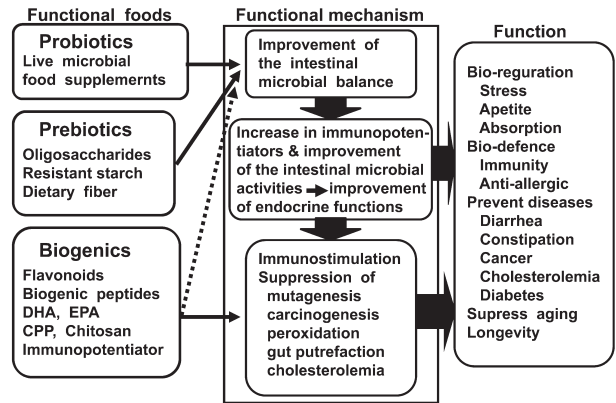


Fig. 21. Functional mechanism of functional foods.

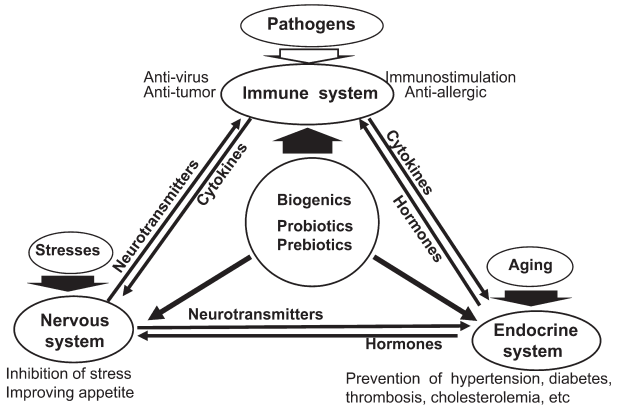


Fig. 22. Maintenance of bio-homeostasis by functional foods.



Fig. 23. Prizes of the results of creation.

arise. Then, a work hypothesis is put forward. An original research subject is chosen from a wide field. It includes the development of an equipment and novel devices for the research, as well as the establishment of the

methodology.

A hypothesis is a hypothesis to the last, and proof (verification) is necessary. Then, the hypothesis develops into a new hypothesis. The recognition is systematized and extends to other genres. Hypothesis is extremely important in research. It is no wonder that hypotheses must be corrected or denied, if they are not proven.

In order to accomplish original research, the foolishness and endurance to support the research over the long term are necessary. However, success or failure, even if all these requirements are filled, is determined by Fate.

I am convinced, that the result of creation is granted to the person with natural talent as a result of repeated efforts with a pure heart, logicity gushing out through insatiable academic curiosity, keen powers of observation, rich experience, and extensive knowledge.

The researcher's way of life

After the World War II, Japan gave priority to economic development for its revival and has finally grown up to be a great economic power. However, it has resulted in environmental destruction, and the Japanese people have come to disregard ethics, education is deteriorating, and shameless, cunning, brutal social events are increasing rapidly. It is indeed regrettable that carelessness, injustice, falsehood, falsification, concealment, swindle, responsibility evasion, and buck-passing are rampant even in the institutions of government. However, there must be no place for them in the life of the researcher.

The researcher's way of life is summarized.

(1) Relevant literature should be closely examined, and always reflected in one's own research.

(2) Experiments must be carefully planned and precisely executed, and the results must represent the truth faithfully without preconception, and without arbitrary or biased views.

(3) Falsehood, fabrication, falsification, appropriation of others' research must never take place.

(4) As a public person, the researcher must act with modesty and uprightly, but must act prudently in order to not be deceived.

CONCLUSION

When looking back on my life, it started in the "school in the sand pit" when I became three years old. In the primary school, I was enthusiastic about making models of fighters, painting posters, and calligraphy, and collecting insect specimens. In high school, I was fortunate to meet good teachers, friends, books, and classical music. While wandering in the forest, I determined that my life should

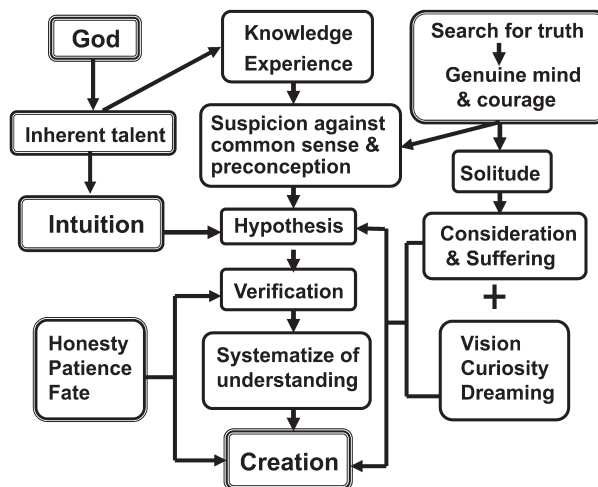


Fig. 24. Process of creation.

be changed by the word which came from Heaven and to entrust everything to Heaven, and to live researching for the truth. I wish to express my gratitude for what I have been able to achieve until today, supported by nature and music, being able to live a life devoted to the pleasure of creation.

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